

**Transcatheter Valve Implantation in Patients with Dysfunctional Left and  
Right Sided Heart Valves**

**NCT02119442**

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## **Statistical Analysis Plan**

Differences in the distributions of baseline continuous variables were tested for significance using the Mann-Whitney U test with a threshold two-sided  $p < 0.05$ . Differences in categorical variables were analyzed with Person's Chi-square or Fisher's exact tests, as appropriate based on sample sizes. Kaplan-Meier curves using log-rank tests were constructed to graphically display time-to-outcome events. Predictor variables were assessed for time-dependent association with endocarditis outcome in univariate Cox proportional hazards regression model. The proportional hazards assumption was assessed graphically with log-log plots with plots for significant associations.

Following the initial analysis using Cox regression, classification and regression tree (CART) methodology was utilized to classify the population into various risk categories for the primary outcome (infective endocarditis). Using the CART methodology, pre-specified variables were entered in the model and subsequent order/splitting was determined by the Gini Index method to partition the data into homogeneously similar subgroups. Validation of the final CART was determined by several methods, including receiver operating characteristic (ROC) curve analysis of the predicted probabilities, the number of correctly classified subjects within the primary cohort as well as cross-validation using a training sample split.